SYNTHESIS OF 1-(3-AZIDO-2,3-DIDEOXY-β-D-*ribo*-HEXOFURANOSYL)-, 1-(2,3-DIDEOXY-β-D-*erythro*-HEXOFURANOSYL)- AND 1-(2,3-DIDEOXY-β-D-*erythro*-HEX-2-ENOFURANOSYL)PYRIMIDINE NUCLEOSIDES

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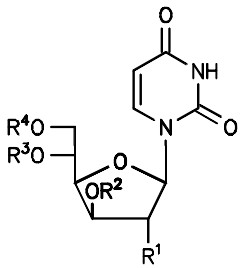
1-(3-Azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)uracil (*XXII*) and 1-(2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)uracil (*VIII*) were prepared starting from 1-(2-*O*-acetyl-3,5,6-tri-*O*-benzoyl-β-D-glucofuranosyl)uracil (*I*) by a procedure described previously for thymine analogs. 1-(2,3-Dideoxy-β-D-*erythro*-hexofuranosyl)uracil (*XIII*) was obtained by catalytic hydrogenation of 1-(5,6-di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)uracil (*VII*) and subsequent methanolysis. Reaction of dibenzoyl derivative *VII*, 1-(5,6-di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hexofuranosyl)uracil (*XII*) and the diacetate prepared by acetylation of azido derivative *XXII* with Lawesson's reagent, followed by methanolysis, afforded 1-(2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)-4-thiouracil (*X*), 1-(2,3-dideoxy-β-D-*erythro*-hexofuranosyl)-4-thiouracil (*XV*) and 1-(3-azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)-4-thiouracil (*XXIII*), respectively. Heating of thio derivatives *X*, *XV* and *XXIII* with methanolic ammonia at 100 °C gave 1-(2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)cytosine (*XI*), 1-(2,3-dideoxy-β-D-*erythro*-hexofuranosyl)cytosine (*XVI*) and 1-(3-azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)cytosine (*XXIV*).

This communication represents a continuation of our previous paper[1] dealing with the synthesis of 1-(2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)thymine, 1(2,3-dideoxy-β-D-*erythro*-hexofuranosyl)thymine and 1-(3-azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)thymine. Although neither of these compounds is active against HIV, the latter one shows a significant activity against HSV-1. The aim of the present study is the synthesis of the above-mentioned analogs with uracil, 4-thiouracil and cytosine as nucleoside bases in order to study how change in the base affects the biological activity.

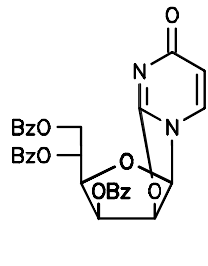
The didehydrodideoxy derivative *VIII* and 3′-azido derivative *XXII* were prepared by a described procedure[1]. The dideoxy analog *XIII* was obtained by catalytic hydrogenation of the protected didehydrodideoxy nucleoside *VII* and subsequent methanolysis with methanolic sodium methoxide. For the conversion of 2′,3′-dideoxyuridine into 2′,3′-dideoxycytidine[2], the method of choice proved to be the synthesis via 4-thio analog which was prepared by reaction of the corresponding uracil derivative with 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide (Lawesson's reagent).

We used this method also for the preparation of cytosine analogs *XI*, *XVI* and *XXIV*. Heating of didehydro derivative *VII* with Lawesson's reagent in 1,2-dichloroethane afforded the 4-thio derivative *IX* in 78% yield. Similarly, we also prepared the 2′,3′-dideoxy-4-thio derivative *XIV* in 97% yield. Methanolysis of the protected nucleosides *IX* and *XIV* with methanolic sodium methoxide gave free nucleosides *X* and *XV*. The azido nucleoside *XXII* was converted into 5′,6′-di-*O*-acetyl derivative which on reaction with Lawesson's reagent and subsequent methanolysis afforded 3′-azido-4-thio derivative *XXIII* in 34% yield. Heating of the thionucleosides *X*, *XV* and *XXII* with methanolic ammonia at 100 °C yielded cytosine nucleosides *XI* (yield 67%), *XVI* (77%) and *XXIV* (57%).

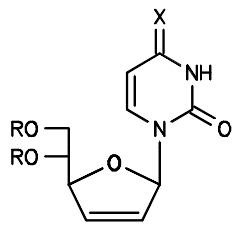
The structures of the compounds synthesized are compatible with their elemental analyses and ^{1}H NMR spectra.



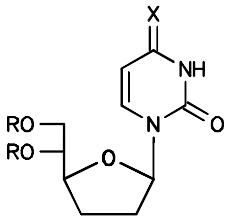
	R^1	R^2	R^3	R^4
I	OAc	Bz	Bz	Bz
II	OH	Bz	Bz	Bz
III	OMs	Bz	Bz	Bz
V	Br	Bz	Bz	Bz
VI	Cl	Bz	Bz	Bz
XVII	H	Bz	Bz	Bz
XVIII	H	H	H	H
XIX	H	H	$C(CH_3)_2$	
XX	H	Ms	$C(CH_3)_2$	



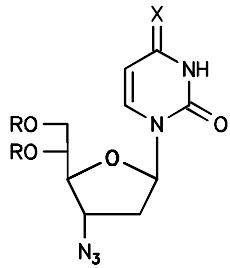
IV



	R	X
VII	Bz	O
VIII	H	O
IX	Bz	S
X	H	S
XI	H	NH



	R	X
XII	Bz	O
XIII	H	O
XIV	Bz	S
XV	H	S
XVI	H	NH



	R	X
XXI	$C(CH_3)_2$	O
XXII	H	O
XXIII	H	S
XXIV	H	NH

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. ^{1}H NMR spectra were obtained with a Varian XL-200 (200 MHz) instrument in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. Chemical shifts are given in ppm (δ-scale) and coupling constants (*J*) in Hz. Column chromatography was performed on silica gel (particle size 30 – 60 μm, Service Laboratories of this Institute). Thin-layer chromatography was carried out on Silufol UV 254 sheets (Kavalier) in the following systems: S1, ethyl acetate–toluene (1 : 1); S2, ethyl acetate; S3, ethyl acetate–acetone–ethanol–water (17 : 3 : 3 : 2). Unless stated otherwise, solvents were evaporated at 40 °C/2kPa and compounds were dried over phosphorus pentoxide at 13 Pa.

1-(2-*O*-Acetyl-3,5,6-tri-*O*-benzoyl-β-D-glucofuranosyl)uracil (*I*)

The title compound *I* (19.5 g, 62%) was prepared from 1,2-di-*O*-acetyl-3,5,6-tri-*O*-benzoyl-D-glucofuranose (28.8 g, 50 mmol) and 2,4-bis(trimethylsilyloxy)pyrimidine (12.0 g, 52.5 mmol) using the procedure described[1] for the preparation of 1-(2-*O*-acetyl-3,5,6-tri-*O*-benzoyl-β-D-glucofuranosyl)-thymine.

The product was obtained as a solid foam, R_F 0.35 (S1). For $C_{33}H_{28}N_2O_{11}$ (628.6) calculated: 63.05% C, 4.49% H, 4.46% N; found: 62.78% C, 4.61% H, 4.25% N. ^{1}H NMR spectrum: 2.14 s, 3 H (2′-$COCH_3$); 4.57 dd, 1 H, *J*(6a′,5′) = 5.7, *J*(6a′,6b′) = 12.3 (H-6a′); 4.88 dd, 1 H, *J*(6b′,5′) = 2.2 (H-6b′); 4.91 dd, 1 H, *J*(4′,3′) = 4.4, *J*(4′,5′) = 8.8 (H-4′); 5.48 dd, 1 H, *J*(2′,1′) = 3.2, *J*(2′,3′) = 1.8 (H-2′); 5.70 dd, 1 H, *J*(5,6) = 8.2, *J* = 1.8 (H-5); 5.81 dd, 1 H (H-3′); 5.88 m, 1 H (H-5′); 6.04 d, 1 H (H-1′); 7.38 – 7.96 m, 16 H (H-6, H arom.); 11.42 s, 1 H (H-3).

1-(3,5,6-Tri-*O*-benzoyl-β-D-glucofuranosyl)uracil (*II*)

A mixture of compound *I* (12.57 g, 20 mmol), 1,4-dioxane (120 ml) and concentrated hydrochloric acid (8 ml) was stirred at room temperature for 2 days. After dilution with ethyl acetate (500 ml), the mixture was washed with water (100 ml) and 5% sodium hydrogen carbonate solution (150 ml), dried over magnesium sulfate and the solvent was evaporated. Chromatography of the residue on silica gel (1.5 kg) in ethyl acetate–toluene (3 : 2) afforded 10.20 g (87%) of nucleoside *II* as a solid foam, R_F 0.24 (S1). For $C_{31}H_{26}N_2O_{10}$ (586.5) calculated: 63.48% C, 4.47% H, 4.78% N; found: 63.28% C, 4.60% H, 4.59% N. ^{1}H NMR spectrum: 4.41 m, 1 H, *J*(2′,OH) = 4.8, *J*(2′,1′) = 1.8, *J*(2′,3′) = 1.5 (H-2′); 4.63 dd, 1 H, *J*(6a′,5′) = 5.5, *J*(6a′,6b′) = 12.5 (H-6a′); 4.89 dd, 1 H, *J*(6b′,5′) = 2.4 (H-6b′); 4.94 dd, 1 H, *J*(4′,3′) = 3.6, *J*(4′,5′) = 9.5 (H-4′); 5.49 dd, 1 H (H-3′); 5.63 d, 1 H, *J*(5,6) = 8.1 (H-5); 5.82 d, 1 H (H-1′); 5.94 m, 1 H (H-5′); 6.44 d, 1 H (2′-OH); 7.39 – 7.99 m, 16 H (H-6, H-arom.); 11.38 s, 1 H (H-3).

1-(3,5,6-Tri-*O*-benzoyl-2-*O*-methanesulfonyl-β-D-glucofuranosyl)uracil (*III*)

Compound *II* (8.80 g 15 mmol) was mesylated by the described[1] procedure to give the title compound *III* (9.47 g, 95%), R_F 0.36 (S1). For $C_{32}H_{28}N_2O_{12}S$ (664.6) calculated: 57.83% C, 4.25% H, 4.22% N, 4.82% S; found: 57.84% C, 4.37% H, 4.20% N, 4.95% S. ^{1}H NMR spectrum: 3.38 s, 3 H (SO_2CH_3); 4.60 dd, 1 H, *J*(6a′,5′) = 5.4, *J*(6a′,6b′) = 12.4 (H-6a′); 4.89 dd, 1 H, *J*(6b′,5′) = 2.3 (H-6b′); 4.98 dd, 1 H, *J*(4′,3′) = 4.2, *J*(4′,5′) = 9.4 (H-4′); 5.64 – 5.72 m, 2 H (H-2′, H-5); 5.87 dd, 1 H, *J*(3′,2′) = 1.9 (H-3′); 5.95 m, 1 H (H-5′); 6.16 d, 1 H, *J*(1′,2′) = 2.4 (H-1′); 7.38 – 7.99 m, 16 H (H-6, H-arom.); 11.48 s, 1 H (H-3).

2,2′-Anhydro-1-(3,5,6-tri-*O*-benzoyl-β-D-mannofuranosyl)uracil (*IV*)

The anhydro derivative *IV* was prepared from mesyl derivative *III* (13.3 g, 20 mmol) by the described[1] procedure; yield 9.8 g (86%) of compound *IV*, m.p. 221 – 222 °C (methanol), R_F 0.49 (S3). For $C_{31}H_{24}N_2O_9$ (568.5) calculated: 65.49% C, 4.26% H, 4.93% N; found: 65.22% C, 4.26% H, 4.91% N. ^{1}H NMR spectrum: 4.46 dd, 1 H, *J*(6a′,5′) = 5.3, *J*(6a′,6b′) = 12.5 (H-6a′); 4.78 dd, 1 H, *J*(6b′,5′) = 2.4 (H-6b′); 4.99 dd, 1 H, *J*(4′,3′) = 4.6, *J*(4′,5′) = 9.3 (H-4′); 5.57 m, 1 H (H-5′); 5.82 t, 1 H, *J*(2′,1′) = 5.9, *J*(2′,3′) = 5.8 (H-2′); 5.94 dd, 1 H (H-3′); 5.95 d, 1 H, *J*(5,6) = 7.3 (H-5); 6.37 d, 1 H (H-1′); 7.33 – 7.91 m, 15 H (H-arom.); 8.02 d, 1 H (H-6).

1-(3,5,6-Tri-*O*-benzoyl-2-bromo-2-deoxy-β-D-glucofuranosyl)uracil (*V*)

Anhydro derivative *IV* (5.7 g, 10 mmol) was treated with 1 M solution of hydrogen bromide in dimethylformamide as described in ref.[1] to give 6.04 g (93%) of bromo derivative *V* as a solid foam, R_F 0.56 (S1). For $C_{31}H_{25}BrN_2O_9$ (649.4) calculated: 57.33% C, 3.88% H, 12.30% Br, 4.31% N; found: 57.52% C, 4.10% H, 12.22% Br, 4.08% N. ^{1}H NMR spectrum: 4.63 dd, 1 H, *J*(6a′,5′) = 5.4, *J*(6a′,6b′) = 12.4 (H-6a′); 4.92 dd, 1 H, *J*(6b′,5′) = 2.4 (H-6b′); 5.02 t, 1 H, *J*(2′,1′) = 2.9, *J*(2′,3′) = 2.2 (H-2′); 5.14 dd, 1 H, *J*(4′,5′) = 9.3, *J*(4′,3′) = 4.0 (H-4′); 5.67 dd, 1 H, *J*(5,6) = 8.2, *J* = 2.1 (H-5); 5.82 dd, 1 H (H-3′); 6.00 m, 1 H (H-5′); 6.30 d, 1 H (H-1′); 7.37 – 8.01 m, 16 H (H-6, H-arom.); 11.43 s, 1 H (H-3).

1-(3,5,6-Tri-*O*-benzoyl-2-chloro-2-deoxy-β-D-glucofuranosyl)uracil (*VI*)

Anhydro derivative *IV* (5.69 g, 10 mmol) was treated with 1 M solution of hydrogen chloride in dimethylformamide under the same conditions as described in ref.[1]. Yield 5.68 g (94%) of chloro derivative *VI* as a solid foam, R_F 0.56 (S1). For $C_{31}H_{25}ClN_2O_9$ (605.0) calculated: 61.54% C, 4.17% H, 5.86%

Cl, 4.63% N; found: 61.39% C, 4.27% H, 5.87% Cl, 4.42% N. ^{1}H NMR spectrum: 4.63 dd, 1 H, *J*(6a′,5′) = 5.4, *J*(6a′,6b′) = 12.4 (H-6a′); 4.92 dd, 1 H, *J*(6b′,5′) = 2.3 (H-6b′); 5.06 t, 1 H, *J*(2′,1′) = 2.4, *J*(2′,3′) = 1.9 (H-2′); 5.11 dd, 1 H, *J*(4′,3′) = 4.0, *J*(4′,5′) = 9.4 (H-4′); 5.66 d, 1 H, *J*(5,6) = 8.2 (H-5); 5.77 dd, 1 H (H-3′); 6.00 m, 1 H (H-5′); 6.17 d, 1 H (H-1′); 7.38 – 8.02 m, 16 H (H-6, H-arom.); 11.43 s, 1 H (H-3).

1-(5,6-Di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)uracil (*VII*)

Bromo derivative *V* (5.19 g, 8 mmol) was converted into the title compound *VII* by the procedure described for the thymine analog[1]; yield 3.05 g (85%) of *VII*, m.p. 193 – 194 °C, R_F 0.18 (S1). For $C_{24}H_{20}N_2O_7$ (448.4) calculated: 64.28% C, 4.50% H, 6.25% N; found: 64.14% C, 4.52% H, 6.32% N. ^{1}H NMR spectrum: 4.56 dd, 1 H, *J*(6a′,5′) = 6.9, *J*(6a′, 6b′) = 12.0 (H-6a′); 4.61 d, 1 H, *J*(5,6) = 8.1 (H-5); 4.76 dd, 1 H, *J*(6b′,5′) = 3.5 (H-6b′); 5.21 m, 1 H (H-4′); 5.60 m, 1 H, *J*(5′,4′) = 3.6 (H-5′); 6.10 m, 1 H, *J*(3′,1′) = 1.8, *J*(3′,2′) = 6.1, *J*(3′,4′) = 1.8 (H-3′); 6.74 m, 1 H, *J*(2′,1′) = 1.8, *J*(2′,4′) = 1.8 (H-2′); 6.81 m, 1 H, *J*(1′,4′) = 3.6 (H-1′); 7.17 d, 1 H (H-6); 7.45 – 7.74 m and 7.88 – 7.97 m, 6 H and 4 H (H-arom.); 11.35 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hex-2-enofuranosyl)uracil (*VIII*)

As described for the thymine derivative[1], methanolysis of benzoyl derivative *VII* (448 mg, 1 mmol) afforded the free nucleoside *VIII* (207 mg, 86%), m.p. 151 – 152 °C, R_F 0.46 (S3). For $C_{10}H_{12}N_2O_5$ (240.2) calculated: 50.00% C, 5.04% H, 11.66% N; found: 50.16% C, 5.05% H, 11.81% N. ^{1}H NMR spectrum: 3.42 t, 2 H, *J*(6′,5′) = 4.9, *J*(6′,OH) = 5.2 (2 × H-6′); 3.59 m, 1 H, *J*(5′,4′) = 4.7, *J*(5′,OH) = 5.3 (H-5′); 4.73 t, 1 H (6′-OH); 4.79 m, 1 H (H-4′); 5.07 d, 1 H (5′-OH); 5.58 d, 1 H, *J*(5,6) = 8.1 (H-5); 5.90 dt, 1 H, *J*(3′,1′) = 1.7, *J*(3′,2′) = 6.1, *J*(3′,4′) = 1.9 (H-3′); 6.48 dt, 1 H, *J*(2′,1′) = 1.8, *J*(2′,4′) = 1.7 (H-2′); 6.79 m, 1 H, *J*(1′,4′) = 3.1 (H-1′); 7.76 d, 1 H (H-6); 11.30 s, 1 H (H-3).

1-(5,6-Di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hex-2-enofuranosyl)-4-thiouracil (*IX*)

A solution of didehydro derivative *VII* (2.24 g, 5 mmol) and Lawesson's reagent (1.23 g, 3 mmol) in dichloroethane (50 ml) was refluxed under argon for 1 h. After cooling, the solvent was evaporated and the residue column chromatographed on silica gel (500 g) in toluene–ethyl acetate (3 : 2). Crystallization from ethanol afforded 1.81 g (78%) of thio derivative *IX*, m.p. 136 – 138 °C, R_F 0.61 (S1). For $C_{24}H_{20}N_2O_6S$ (464.5) calculated: 62.06% C, 4.34% H, 6.03% N, 6.90% S; found: 61.94% C, 4.31% H, 5.94% N, 7.01% S. ^{1}H NMR spectrum: 4.56 dd, 1 H, *J*(6a′,5′) = 6.9, *J*(6a′,6b′) = 12.0 (H-6a′); 4.76 dd, 1 H, *J*(6b′,5′) = 3.5 (H-6b′); 5.21 – 5.28 m, 1 H (H-4′); 5.34 d, 1 H, *J*(5,6) = 7.3 (H-5); 5.60 m, 1 H (H-5′); 6.11 m, 1 H, *J*(3′,1′) = 2.0, *J*(3′,2′) = 5.4 (H-3′); 6.75 – 6.78 m, 2 H (H-2′, H-1′); 7.07 d, 1 H (H-6); 7.45 – 7.75 m and 7.88 – 7.97 m, 6 H and 4 H (H-arom.); 12.73 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hex-2-enofuranosyl)-4-thiouracil (*X*)

Benzoyl derivative *IX* (464 mg, 1 mmol) was added to 0.25 M methanolic sodium methoxide and the mixture was stirred until it became homogeneous. After standing at room temperature overnight, the mixture was neutralized with Dowex 50 (H^+ form), the solvent was evaporated and the residue chromatographed on a column of silica gel (45 g) in ethyl acetate. Crystallization from ethyl acetate afforded 196 mg (76%) of the free nucleoside *X*, m.p. 135 – 138 °C, R_F 0.22 (S2). For $C_{10}H_{12}N_2O_4S$ (256.3) calculated: 46.86% C, 4.72% H, 10.93% N, 12.51% S; found: 46.68% C, 4.69% H, 10.96% N, 12.29% S. ^{1}H NMR spectrum: 3.42 t, 2 H, *J*(6′,5′) = 5.4, *J*(6′,OH) = 5.5 (2 × H-6′); 3.60 m, 1 H, *J*(5′,4′) = 5.4, *J*(5′,OH) = 5.4 (H-5′); 4.73 t, 1 H (6′-OH); 4.82 m, 1 H (H-4′); 5.08 d, 1 H (5′-OH);

5.93 dt, 1 H, *J*(3′,1′) = 1.5, *J*(3′,2′) = 5.8, *J*(3′,4′) = 2.3 (H-3′); 6.25 d, 1 H, *J*(5,6) = 7.5; (H-5); 6.51 dt, 1 H, *J*(2′,1′) = 1.6, *J*(2′,4′) = 1.4 (H-2′); 6.76 m, 1 H, *J*(1′,4′) = 3.0 (H-1′); 7.68 d, 1 H (H-6); 12.71 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hex-2-enofuranosyl)cytosine (*XI*)

A suspension of benzoyl derivative *IX* (989 mg, 1 mmol) in methanolic ammonia (saturated at 0 °C) was heated in an autoclave at 100 °C for 2.5 h. The resulting solution was concentrated to a half and allowed to stand at 5 °C overnight. The crystalline cytosine derivative *XI* was filtered and washed with methanol; yield 320 mg (67%), m.p. 193 – 194 °C, R_F 0.10 (S3). For $C_{10}H_{13}N_3O_4$ (239.2) calculated: 50.20% C, 5.48% H, 17.57% N; found: 49.96% C, 5.40% H, 17.72% N. ^{1}H NMR spectrum: 3.38 – 3.60 m, 3 H (H-5′, 2 × H-6′); 4.69 t, 1 H, *J*(OH,6′) = 5.6 (6′-OH); 4.71 – 4.76 m, 1 H (H-4′); 5.01 d, 1 H, *J*(OH,5′) = 5.2 (5′-OH); 5.67 d, 1 H, *J*(5,6) = 7.4 (H-5); 5.86 dt, 1 H, *J*(3′,1′) = 1.7, *J*(3′,2′) = 6.0, *J*(3′,4′) = 2.0 (H-3′); 6.41 dt, 1 H, *J*(2′,1′) = 1.8, *J*(2′,4′) = 1.6 (H-2′); 6.86 m, 1 H, *J*(1′,4′) = 3.0 (H-1′); 7.14 – 7.17 bd, 2 H (NH_2); 7.70 d, 1 H (H-6).

1-(5,6-Di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hexofuranosyl)uracil (*XII*)

Derivative *VII* (673 mg, 1.5 mmol) was hydrogenated in dimethylformamide (5 ml) over 10% Pd on activated carbon (70 mg) for 4 h. The catalyst was then removed by filtration through Celite, washed with dimethylformamide and the combined filtrates were concentrated. The residue was dissolved in chloroform and chromatographed on a column of silica gel (25 g) in ethyl acetate. Crystallization from ethanol afforded 601 mg (89%) of product *XII*, m.p. 167 – 168 °C, R_F 0.16 (S1). For $C_{24}H_{22}N_2O_7$ (450.4) calculated: 63.99% C, 4.92% H, 6.22% N; found: 64.16% C, 4.94% H, 6.08% N. ^{1}H NMR spectrum: 1.98 – 2.20 m, 2.31 – 2.42 m, 4 H (2 × H-2′, 2 × H-3′); 4.38 m, 1 H (H-4′), Σ*J* = 19.2); 4.49 dd, 1 H, *J*(6a′,5′) = 6.4, *J*(6a′,6b′) = 12.2 (H-6a′); 4.75 dd, 1 H, *J*(6b′,5′) = 3.0 (H-6b′); 5.11 d, 1 H, *J*(5,6) = 7.9 (H-5); 5.69 m, 1 H, *J*(5′,4′) = 9.4 (H-5′); 6.04 dd, 1 H, *J*(1′,2a′) = 3.6, *J*(1′,2b′) = 7.6 (H-1′); 7.46 – 7.72 m and 7.89 – 8.01 m, 7 H and 4 H (H-6, H-arom.); 11.29 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hexofuranosyl)uracil (*XIII*)

Benzoyl derivative *XII* (225 mg, 0.5 mmol) was methanolyzed in the same manner as described for compound *VIII*. Crystallization from 2-propanol afforded 105 mg (87%) of dideoxynucleoside *XIII*, m.p. 172 – 173 °C, R_F 0.33 (S3). For $C_{10}H_{14}N_2O_5$ (242.2) calculated: 49.58% C, 5.83% H, 11.57% N; found: 49.36% C, 5.78% H, 11.46% N. ^{1}H NMR spectrum: 1.77 – 1.98 m and 2.12 – 2.37 m, 4 H (2 × H-2′, 2 × H-3′); 3.34 t, 2 H, *J*(6′,5′) = *J*(6′,OH) = 6.1 (2 × H-6′); 3.70 – 3.80 m, 1 H (H-5′); 3.97 – 4.06 m, 1 H (H-4′); 4.64 t, 1 H (6′-OH); 5.09 d, 1 H, *J*(OH,5′) = 5.1 (5′-OH); 5.56 d, 1 H, *J*(5,6) = 8.0 (H-5); 8.00 d, 1 H (H-6); 11.24 s, 1 H (H-3).

1-(5,6-Di-*O*-benzoyl-2,3-dideoxy-β-D-*erythro*-hexofuranosyl)-4-thiouracil (*XIV*)

Lawesson's reagent (364 mg, 0.9 mmol) was added to a solution of dideoxy derivative *XII* (676 mg, 1.5 mmol) in dichloroethane (15 ml) and the mixture was refluxed for 1 h under argon. After concentration to about 5 ml, the residue was chromatographed on a column of silica gel (100 g) in toluene–ethyl acetate (2 : 1). The thio derivative *XIV* (681 mg, 97%) was obtained as a solid foam, R_F 0.62 (S1). For $C_{24}H_{22}N_2O_6S$ (466.5) calculated: 61.79% C, 4.75% H, 6.01% N, 6.87% S; found: 61.71% C, 4.94% H, 5.91% N, 6.87% S. ^{1}H NMR spectrum: 2.00 – 2.46 m, 4 H (2 × H-2′, 2 × H-3′); 4.38 – 4.46 m, 1 H (H-4′); 4.50 dd, 1 H, *J*(6a′,5′) = 6.4, *J*(6a′,6b′) = 12.2 (H-6a′); 4.76 dd, 1 H,

J(6b′,5′) = 3.1 (H-6b′); 5.71 m, 1 H, *J*(5′,4′) = 4.8 (H-5′); 5.78 dd, 1 H, *J*(5,6) = 7.3, *J* = 1.8 (H-5); 5.99 dd, 1 H, *J*(1′,2a′) = 2.4, *J*(1′,2b′) = 7.0 (H-1′); 7.42 d, 1 H (H-6); 7.50 – 7.74 m and 7.89 – 8.01 m, 6 H and 4 H (H-arom.); 12.65 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hexofuranosyl)-4-thiouracil (*XV*)

A solution of benzoyl derivative *XIV* (466 mg, 1 mmol) in 0.25 M methanolic sodium methoxide (10 ml) was set aside at room temperature overnight. After neutralization with Dowex 50 (H^+ form), the solvent was evaporated and the residue crystallized from 2-propanol–methanol; yield 180 mg (70%) of compound *XV*, m.p. 167 – 169 °C, R_F 0.19 (S2). For $C_{10}H_{14}N_2O_4S$ (258.3) calculated: 46.50% C, 5.46% H, 10.85% N, 12.41% S; found: 46.48% C, 5.40% H, 10.92% N, 12.43% S. ^{1}H NMR spectrum: 1.78 – 2.39 m, 4 H (2 × H-2′, 2 × H-3′); 3.35 t, 2 H, *J*(6′,5′) = 5.7, *J*(6′,OH) = 5.5 (2 × H-6′); 3.80 m, 1 H, *J*(5′,4′) = 3.8 (H-5′); 4.06 m, 1 H, *J*(4′,3a′) = *J*(4′,3b′) = 7.6 (H-4′); 4.65 t, 1 H (6′-OH); 5.14 d, 1 H, *J*(OH,5′) = 5.4 (5′-OH); 5.88 dd, 1 H, *J*(1′,2a′) = 2.6, *J*(1′,2b′) = 6.7 (H-1′); 6.25 dd, 1 H, *J*(5,6) = 7.6, *J* = 1.5 (H-5); 7.99 d, 1 H (H-6); 12.65 s, 1 H (H-3).

1-(2,3-Dideoxy-β-D-*erythro*-hexofuranosyl)cytosine (*XVI*)

A suspension of thio derivative *XV* (517 mg, 2 mmol) in methanolic ammonia (20 ml, saturated at 0 °C) was heated in an autoclave at 100 °C for 2 h. The reaction mixture was then concentrated to a half of the original volume and allowed to stand at 5 °C overnight. The crystalline compound *XVI* was collected (262 mg, 54%) and washed with methanol. The residue after evaporation of the mother liquors was chromatographed on a column of silica gel (15 g) in ethyl acetate–acetone–ethanol–water (14 : 3 : 4 : 4). Crystallization from methanol afforded further 110 mg (23%) of compound *XVI*, m.p. 187 – 187.5 °C, R_F 0.10 (S3). For $C_{10}H_{15}N_3O_4$ (241.2) calculated: 49.78% C, 6.27% H, 17.42% N; found: 49.50% C, 6.17% H, 17.61% N. ^{1}H NMR spectrum: 1.74 – 1.89 m and 2.11 – 2.32 m, 4 H (2 × H-2′, 2 × H-3′); 3.34 t, 2 H (2 × H-6′); 3.70 – 3.81 m, 1 H (H-5′); 3.94 – 4.03 m, 1 H (H-4′); 4.64 t, 1 H, *J*(OH,6′) = 5.6 (6′-OH); 5.07 d, 1 H, *J*(OH,5′) = 5.2 (5′-OH); 5.66 d, 1 H, *J*(5,6) = 7.3 (H-5); 5.91 dd, 1 H, *J*(1′,2a′) = 2.8, *J*(1′,2b′) = 6.4 (H-1′); 7.04 bs, 2 H (NH_2); 7.97 d, 1 H (H-6); after exchange with D_2O: 3.34 d, 2 H, *J*(6′,5′) = 5.6 (2 × H-6′).

1-(3,5,6-Tri-*O*-benzoyl-2-deoxy-β-D-*arabino*-hexofuranosyl)uracil (*XVII*)

Chloro derivative *VI* (6.05 g, 10 mmol) was reduced with tributylstannane as described for the thymine analog[1]. Crystallization from 2-propanol gave 4.91 g (86%) of deoxynucleoside *XVII*, m.p. 199 – 200 °C, R_F 0.36 (S1). For $C_{31}H_{26}N_2O_9$ (570.5) calculated: 65.26% C, 4.59% H, 4.91% N; found: 65.40% C, 4.47% H, 4.85% N. ^{1}H NMR spectrum: 2.33 dd, 1 H, *J*(2a′,1′) = 2.0, *J*(2a′,2b′) = 15.5 (H-2a′); 2.96 m, 1 H, *J*(2b′,1′) = 7.8, *J*(2b′,3′) = 4.9 (H-2b′); 4.59 dd, 1 H, *J*(6a′,5′) = 5.1, *J*(6a′,6b′) = 12.4 (H-6a′); 4.74 dd, 1 H, *J*(4′,3′) = 3.4, *J*(4′,5′) = 9.3 (H-4′); 4.91 dd, 1 H, *J*(6b′,5′) = 2.2 (H-6b′); 5.63 d, 1 H, *J*(5,6) = 7.8 (H-5); 5.77 dd, 1 H (H-3′); 5.89 m, 1 H (H-5′); 6.21 dd, 1 H (H-1′); 7.40 – 8.00 m, 16 H (H-6, H-arom.); 11.31 s, 1 H (H-3).

1-(2-Deoxy-β-D-*arabino*-hexofuranosyl)uracil (*XVIII*)

Methanolysis of benzoyl derivative *XVII* (5.71 g, 10 mmol) with 0.1 M methanolic sodium methoxide afforded compound *XVIII* (2.10 g, 81%), m.p. 199 – 201 °C, R_F 0.31 (S3). For $C_{10}H_{14}N_2O_6$ (258.2) calculated: 46.51% C, 5.46% H, 10.85% N; found: 46.53% C, 5.41% H, 10.81% N. ^{1}H NMR spectrum: 1.86 dd, 1 H, *J*(2a′,1′) = 1.5, *J*(2a′,2b′) = 14.7 (H-2a′); 2.54 m, 1 H, *J*(2b′,1′) = 8.4, *J*(2b′,3′) = 5.1 (H-2b′); 3.39 m, 1 H, *J*(6a′,5′) = 5.1, *J*(6a′,6b′) = 10.2, *J*(6a′,OH) = 5.1 (H-6a′); 3.54 – 3.64 m, 2 H

(H-6′, H-4′); 3.69 m, 1 H, Σ*J* = 21.1 (H-5′); 4.27 m, 1 H (H-3′); 4.50 t, 1 H (6′-OH); 4.71 d, 1 H, *J*(OH,5′) = 5.8 (5′-OH); 5.21 d, 1 H, *J*(OH,3′) = 2.3 (3′-OH); 5.63 d, 1 H, *J*(5,6) = 8.2 (H-5); 6.03 dd, 1 H (H-1′); 7.92 d, 1 H (H-6); 11.22 s, 1 H (H-3).

1-(2-Deoxy-5,6-*O*-isopropylidene-β-D-*arabino*-hexofuranosyl)uracil (*XIX*)

The title compound was prepared from 2′-deoxynucleoside *XVIII* (1.29 g, 5 mmol) by a described[1] procedure. Crystallization from 2-propanol gave 1.31 g (88%) of derivative *XIX*, m.p. 179 – 182 °C, R_F 0.38 (S2). For $C_{13}H_{18}N_2O_6$ (298.3) calculated: 52.34% C, 6.08% H, 9.39% N; found: 52.08% C, 5.91% H, 9.12% N. ^{1}H NMR spectrum: 1.28 s and 1.32 s, 6 H ($C(CH_3)_2$); 1.87 dd, 1 H, *J*(2a′,1′) = 2.1, *J*(2a′,2b′) = 15.0 (H-2a′); 2.60 m, 1 H, *J*(2b′,1′) = 8.8, *J*(2b′,3′) = 5.0 (H-2b′); 3.74 dd, 1 H, *J*(4′,3′) = 2.8, *J*(4′,5′) = 8.3 (H-4′); 3.83 dd, 1 H, *J*(6a′,5′) = 5.8, *J*(6a′,6b′) = 8.5 (H-6a′); 4.04 dd, 1 H, *J*(6b′,5′) = 6.4 (H-6b′); 4.23 m, 1 H (H-3′); 4.35 m, 1 H (H-5′); 5.56 d, 1 H, *J*(OH,3′) = 3.7 (3′-OH); 5.66 d, *J*(5,6) = 8.2 (H-5); 6.11 dd, 1 H (H-1′); 7.92 d, 1 H (H-6); 11.27 s, 1 H (H-3).

1-(2-Deoxy-5,6-*O*-isopropylidene-3-*O*-methanesulfonyl-β-D-arabino-hexofuranosyl)uracil (*XX*)

Isopropylidene derivative *XIX* (1.46 g, 5 mmol) was converted into the title compound *XX* by a described[1] procedure. Crystallization from 2-propanol–methanol afforded 1.54 g (82%) of the mesyl derivative *XX*, m.p. 190 – 193 °C, R_F 0.49 (S2). For $C_{14}H_{20}N_2O_8S$ (376.4) calculated: 44.67% C, 5.36% H, 7.44% N, 8.52% S; found: 44.52% C, 5.28% H, 7.60% N, 8.57% S. ^{1}H NMR spectrum: 1.29 s and 1.35 s, 2 × 3 H ($C(CH_3)_2$); 2.28 dd, 1 H, *J*(2a′,1′) = 3.0, *J*(2a′,2b′) = 16.0 (H-2a′); 2.89 m, 1 H, *J*(2b′,1′) = 8.3, *J*(2b′,3′) = 5.5 (H-2b′); 3.24 s, 3 H (CH_3SO_2); 3.87 dd, 1 H, *J*(6a′,5′) = 5.2, *J*(6a′,6b′) = 8.4 (H-6a′); 4.01 – 4.13 m, 2 H (H-6b′,H-4′); 4.37 m, 1 H, *J*(5′,4′) = 7.3, *J*(5′,6b′) = 5.8 (H-5′); 5.25 dd, 1 H, *J*(3′,4′) = 3.2 (H-3′); 5.68 dd, 1 H, *J*(5,6) = 8.3, *J* = 2.0 (H-5); 6.13 dd, 1 H (H-1′); 7.51 d, 1 H (H-6); 11.37 s, 1 H (H-3).

1-(3-Azido-2,3-dideoxy-5,6-*O*-isopropylidene-β-D-*ribo*-hexofuranosyl)uracil (*XXI*)

Mesyl derivative *XX* (3.76 g, 10 mmol) was treated with lithium azide in dimethylformamide according to ref.[1]. Crystallization from 2-propanol gave 2.48 g (77%) of azido derivative *XXI*, m.p. 143 – 146 °C. For $C_{13}H_{17}N_5O_5$ (323.3) calculated: 48.29% C, 5.30% H, 21.66% N; found: 48.43% C, 5.29% H, 21.41% N. ^{1}H NMR spectrum: 1.30 s and 1.38 s, 2 × 3 H ($C(CH_3)_2$); 2.19 – 2.47 m, 2 H (2 × H-2′); 3.73 – 3.82 m, 2 H (H-6a′, H-4′); 4.07 dd, 1 H, *J*(6b′,5′) = 6.6, *J*(6b′,6a′) = 8.8 (H-6b′); 4.23 m, 1 H, *J*(5′,4′) = 6.6, *J*(5′,6a′) = 4.8, *J*(5′,6b′) = 6.6 (H-5′); 4.45 m, 1 H, *J*(3′,2a′) = 4.6, *J*(3′,2b′) = 7.0, *J*(3′,4′) = 4.5 (H-3′); 5.65 d, 1 H, *J*(5,6) = 8.0 (H-5); 6.07 t, 1 H, *J*(1′,2a′) = *J*(1′,2b′) = 6.9 (H-1′); 7.65 d, 1 H (H-6); 11.37 s, 1 H (H-3).

1-(3-Azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)uracil (*XXII*)

A solution of isopropylidene derivative *XXI* (1.63 g, 5 mmol) in 80% aqueous methanol (25 ml) was stirred at 80 °C with Dowex 50 (H^+ form, 2 ml of wet resin) for 40 min. The ion-exchanger was filtered off, washed with methanol and the combined filtrates were concentrated. Crystallization of the residue from water afforded 1.13 g (80%) of compound *XXII*, m.p. 151 – 152 °C, R_F 0.71 (S3). For $C_{10}H_{13}N_5O_5$ (283.2) calculated: 42.40% C, 4.63% H, 24.73% N; found: 42.42% C, 4.47% H, 24.91% N. ^{1}H NMR spectrum: 2.16 – 2.39 m, 2 H (2 × H-2′); 3.44 t, 2 H, *J*(6′,5′) = 5.3, *J*(6′,OH) = 5.3 (2 × H-6′); 3.65 m, 1 H, *J*(5′,4′) = 4.2, *J*(5′,OH) = 5.3 (H-5′); 3.88 t, 1 H, *J*(4′,3′) = 4.2 (H-4′); 4.49 m, 1 H, *J*(3′,2a′) = 4.2, *J*(3′,2b′) = 6.2 (H-3′); 4.72 t, 1 H (6′,OH); 5.30 d, 1 H (5′-OH); 5.64 dd, 1 H,

J(5,6) = 8.1, J = 2.0 (H-5); 6.06 t, 1 H, J(1′,2a′) = J(1′,2b′) = 6.9 (H-1′); 7.90 d, 1 H (H-6); 11.35 s, 1 H (H-3).

1-(3-Azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)-4-thiouracil (*XXIII*)

A mixture of azido derivative *XXII* (566 mg, 2 mmol), acetonitrile (10 ml), acetic anhydride (1 ml) and 4-(dimethylamino)pyridine (50 mg) was stirred until it became homogeneous, the solution was stirred at room temperature for addidional 30 min, methanol (1 ml) was added and after 10 min the solvent was evaporated. The residue was dissolved in dichloroethane (20 ml) and refluxed under argon with Lawesson's reagent (500 mg) for 45 min. The mixture was concentrated to a quarter of the original volume, the residue applied onto a column of silica gel (130 g) and eluted with ethyl acetate–toluene (2 : 3). The UV-absorbing fraction was concentrated and the residue was dissolved in 0.2 M methanolic sodium methoxide (10 ml). After standing at room temperature for 4 h, the solution was neutralized with Dowex 50 (H^+ form), the ion exchanger was filtered off, washed with methanol and the combined filtrates were evaporated. Chromatography of the residue on a column of silica gel (20 g) in ethyl acetate afforded 201 mg (34%) of compound *XXIII* as a solid foam, R_F 0.65 (S2). For $C_{10}H_{13}N_5O_4S$ (299.3) calculated: 40.13% C, 4.38% H, 23.40% N, 10.71% S; found: 40.42% C, 4.53% H, 23.09% N, 10.39% S. ^{1}H NMR spectrum: 2.21 – 2.42 m, 2 H (2 × H-2′); 3.44 t, 2 H, J(6′,OH) = 5.5, J(6′,5′) = 5.2 (2 × H-6′); 3.68 m, 1 H, J(5′,OH) = 5.2, J(5′,4′) = 4.3 (H-5′); 3.91 t, 1 H, J(4′,3′) = 4.3 (H-4′); 4.49 m, 1 H, J(3′,2a′) = 4.6, J(3′,2b′) = 6.7 (H-3′); 4.74 t, 1 H (6′-OH); 5.32 d, 1 H (5′-OH); 6.00 t, 1 H, J(1′,2a′) = 6.6, J(1′,2b′) = 6.7 (H-1′); 6.29 d, 1 H, J(5,6) = 7.6 (H-5); 7.72 d, 1 H (H-6); 12.68 s, 1 H (H-3).

1-(3-Azido-2,3-dideoxy-β-D-*ribo*-hexofuranosyl)cytosine (*XXIV*)

A solution of thio derivative *XXIII* (150 mg, 0.5 mmol) in methanolic ammonia (5 ml) was heated at 100 °C for 40 min in an autoclave. The solution was evaporated and the residue chromatographed on silica gel column in ethyl acetate–acetone–ethanol–water (14 : 3 : 4 : 4); yield 81 mg (57%) of cytosine derivative *XXIV*, R_F 0.28 (S3). For $C_{10}H_{14}N_6O_4$ (282.3) calculated: 42.55% C, 5.00% H, 29.78% N; found: 42.30% C, 4.81% H, 29.49% N. ^{1}H NMR spectrum: 2.10 – 2.32 m, 2 H (2 × H-2′); 3.29 – 3.53 m, 2 H (2 × H-6′); 3.64 m, 1 H, J(5′,6a′) = J(5′,6b′) = J(5′,OH) = 4.9, J(5′,4′) = 4.6 (H-5′); 3.87 dd, 1 H, J(4′,3′) = 3.7 (H-4′); 4.46 m, 1 H, J(3′,2a′) = 6.5, J(3′,2b′) = 3.8 (H-3′); 4.71 bt, 1 H (6′-OH); 5.27 d, 1 H (5′-OH); 5.74 d, 1 H, J(5,6) = 7.3 (H-5); 6.07 t, 1 H, J(1′,2a′) = 7.0, J(1′,2b′) = 6.7 (H-1′); 7.25 bd, 2 H (NH_2); 7.74 d, 1 H (H-6).

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